REMARKS

A check for the fee for a one month extension of time and for a Supplemental Information Disclosure Statement accompanies this response. Any fees that may be due in connection with filing this paper or with this application during its entire pendency may be charged to Deposit Account No. 50-1213. If a Petition for extension of time is required, this paper is to be considered such Petition, and any fee charged to Deposit Account No. 50-1213. Claims 8-14 and 58-72 are pending in this application. Claim 8 is amended to correct minor typographical errors and to more particularly point out the claimed subject matter. The amendments find basis in the specification, *e.g.*, at page 3, lines 10-28, at page 7, lines 11-17 and at page 15, line 30, through page 16, line 6. Claim 14 is correspondingly amended to provide proper antecedent basis in claim 8.

Claim 8 also is amended more clearly recite that the methods assigns a previously unknown function to a sequence of nucleotides. Basis for this amendment can be found throughout the specification, which discloses methods for the determination of heretofore unknown function(s) of the products encoded by sample nucleic acid molecules of known sequence, such as sequences of genes, gene fragments and essential sequence tags (ESTs) contained in sequence databases compiled from various genome sequencing projects. As disclosed in the instant application (*e.g.*, at page 3, line 10, through page 4, line 4; at page 4, lines 29-32; at page 7, lines 3-20; page 16, lines 20-23; and Example 1, beginning on page 17, line 13), a family of related oligonucleotides is prepared based upon the known sample nucleic acid sequence. The oligonucleotide family, as described in the instant application, includes nucleic acid members that are related to the known sample nucleic acid of unknown function and encode an antisense RNA, a ribozyme, a polypeptide or a fusion

polypeptide (see, *e.g.*, the specification at page 4, lines 29-32). The members of this oligonucleotide family are expressed as individual transcription products in a host cell and phenotypic changes within the resulting host cells are detected and analyzed (see, *e.g.*, page 3, lines 13-26; page 4, line 32, through page 5, line 3; page 15, line 3, through page 17, line 2; Example 4, beginning at page 19, line 6; and Example 7, beginning at page 20, line 24). The phenotypic changes are then correlated to the sample nucleic acid, thereby assigning a function to the sample nucleic acid sequence.

Claims 58, 62 and 64-69 are amended and claims 70-72 added to correct inadvertent dependency errors. The amendment of claim 58 (and added claims 70-72) finds basis in claim 8, which provides antecedent basis for one or more members of an oligonucleotide family, in the claims as originally filed and in the specification, *e.g.*, at page 6, lines 22-30 and at page 7, line 32, through page 8, line 7. The amendment of claim 62 finds basis in any of claims 58-61, which provide antecedent basis for an expression vector, in the claims as originally filed and in the specification, *e.g.*, at page 4, lines 24-32, at page 5, line 18, through page 6, line 8, in Example 2, beginning at page 18, line 4 and in Example 5, beginning at page 19, line 29. The amendment of claim 64 finds basis in claim 58, which provides antecedent basis for an expression vector, in the claims as originally filed and in the specification, *e.g.*, at page 13, lines 18-22, in Example 3, beginning at page 18, line 21 and in Example 6, at page 20, line 10. The amendment of claim 65 finds basis in claim 8, which provides antecedent basis for a sample nucleic acid, in the claims as originally filed and in the specification, *e.g.*, at page 4, lines 29-32 and at page 5, lines 7-10. The amendment of claim 66 finds basis in claim 8, which provides antecedent basis for a family of oligonucleotides, in the claims as originally filed and in the specification, *e.g.*, at page 7, lines 15-17. The amendment of claim 67 finds basis in claim 8, which

provides antecedent basis for a member of the family of oligonucleotides, in the claims as originally filed and in the specification, *e.g.*, at page 5, lines 13-17 and at page 15, line 30, through page 16, line 10. The amendment of claims 68 and 69 finds basis in the claims as originally filed and in the specification, *e.g.*, at page 4, lines 24-33 and page 6, lines 12-22. No amendments have been made to obviate prior art and no new matter has been added.

A marked up copy per 37 C.F.R. §1.121 of the amended claims is attached to this response.

ELECTION/RESTRICTIONS

The Office Action alleges that added claims 58-69, submitted Responsive to the Restriction Requirement, filed October 25, 2002, are directed to subject matter that is independent or distinct from the originally claimed subject matter. The Office Action further alleges that because claims 58-69 depend from claim 1, which was cancelled in the Applicant's previous Response, they are withdrawn from consideration as being directed to a non-elected subject matter.

Claims 58, 62 and 64-69 are amended herein to correct inadvertent dependency errors. Claims 58-69 now depend on claim 8, which is pending in the instant application. Thus, the pending claims are directed to the elected subject matter. Accordingly, Applicant has retained withdrawn claims 58-69 pending consideration of the aforementioned inadvertent dependency errors. Reconsideration of the withdrawal of claims 58-69 is respectfully requested.

THE OBJECTION TO CLAIM 8

Claim 8 is objected to because of an informality in the claim language. The Office Action indicates that a comma has been duplicated in line 4 of the claim. This objection has been rendered moot by amending claim 8 to remove the second occurrence of the comma.

THE REJECTION OF CLAIMS 8-14 UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 8-14 are rejected under 35 U.S.C. § 112, second paragraph for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicant regards as the invention. Specifically, the Office Action alleges that claims 8-14 are indefinite for reciting the phrase "altered functions(s)." The Office Action alleges that the term "altered function(s)" is not defined by the claim, that the specification does not provide a standard for ascertaining the requisite degree and that one of ordinary skill in the art would not be reasonably apprised of the scope of the claimed subject matter. Reconsideration of this rejection is respectfully requested in view of the amendments herein and the following remarks.

RELEVANT LAW

Claims are not read in a vacuum but instead are considered in light of the specification and the general understanding of the skilled artisan. *Rosemount Inc. v. Beckman Instruments, Inc.*, 727 F.2d 1540, 1547, 221 USPQ 1, 7 (Fed. Cir. 1984), *Caterpillar Tractor Co. v. Berco, S.P.A.*, 714 F.2d 1110, 1116, 219 USPQ 185, 188 (Fed. Cir. 1983). When one skilled in the art would understand all of the language in the claims when read in light of the specification, a claim is not indefinite.

There are no requirements for terms to be defined in the claims when one of skill in the art can readily determine the meaning of the term based on the description and definitions provided in the specification. In this respect, an applicant is entitled to be its own lexicographer [see, *e.g.*, MPEP 2111.01 "Applicant may be his or her own lexicographer as long as the meaning assigned to the term is not repugnant to the term's well known usage and utilize terms within the claims that are clear from a reading of the specification. *In re Hill*, 73 USPQ 482 (CCPA 1947)."]. When applicant has provided definitions in the specification, the claims are interpreted in light of such definition.

35 U.S.C. § 112, second paragraph requires only reasonable precision in delineating the bounds of the claimed invention. Claim language is satisfactory if it reasonably apprises those of skill in the art of the bounds of the claimed invention and is as precise as the subject matter permits. *Shatterproof Glass Corp. v. Libby-Owens Ford Col.*, 758 F.2d 613, 624, 225 USPQ 634, 641 (Fed. Cir.), cert. dismissed, 106 S.Ct. 340 (1985).

The amount of detail required to be included in the claims depends on the particular subject matter and the prior art and is not to be viewed in the abstract, but in conjunction with whether the specification is in compliance with the first paragraph of 35 U.S.C. § 112. If the claims, read in light of the specification, reasonably apprise those skilled in the art of the utilization and scope of the invention, and if the language is as precise as the subject matter permits, the courts can demand no more:

> [i]t is not necessary that a claim recite each and every element needed for the practical utilization of the claimed subject matter (*Bendix Corp. v United States*, 600 F.2d 1364, 1369, 220 Ct. Cl. 507, 514, 204 USPQ 617, 621 (1979); See, also, *Carl Zeiss Stiftung v. Renishaw plc*, 20 USPQ2d 1094, 1101).

ANALYSIS

Claim 8 is amended to more particularly point out the claimed subject matter. As amended, claim 8 recites "a corresponding change in function." This amendment finds basis in the specification, *e.g.*, at page 3, lines 26-28 and at page 15, line 30, through page 16, line 6. The cited passage(s) describe methods to identify and assign a function to a sample nucleotide sequence by analyzing cellular phenotypic changes and correlating these changes to the sample nucleic acid. Further, the cited passage(s) describe exemplary phenotypic changes, such as apoptosis, virus titers and altered resistance of the cells to various drugs, which can be correlated to a function of the sample nucleic acid.

Thus, the language of claim 8 is sufficiently clear so that one of skill in the art would understand the metes and bounds of the claim as read in light of the specification and the antecedent basis in the claim. Therefore, claim 8 and claims dependent thereon (claims 9-14 and retained claims 58-69) are not indefinite.

THE REJECTION OF CLAIMS 8-14 UNDER 35 U.S.C. §102(e)

Claims 8-14 are rejected under 35 U.S.C. § 102(e) as being anticipated by Beach *et al.* (US 6,255,071). It is alleged that Beach *et al.* discloses methods for the identification and isolation of nucleic acid molecules, including antisense nucleic acid molecules, based upon their ability to complement a mammalian cellular phenotype. The Office Action further alleges that the disclosed antisense methods for identifying new nucleic acid sequences include steps of introducing and expressing test nucleic acid sequences in cells, followed by assaying the cells for a change in phenotype and isolating new nucleic acid sequences based upon the observation that a loss of an unknown gene produces a particular phenotype. This rejection is respectfully traversed.

RELEVANT LAW

Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration. In re Spada, 15 USPQ2d 1655 (Fed. Cir, 1990), In re Bond, 15 USPQ 1566 (Fed. Cir. 1990), Soundscriber Corp. v. U.S.. 360 F.2d 954, 148 USPQ 298, 301, adopted 149 USPQ 640 (Ct. Cl.) 1966. See, also, Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236, 9 USPQ2d 1913,1920 (Fed. Cir.), cert. denied, 110 S.Ct. 154 (1989). "[A]ll limitations in the claims must be found in the reference, since the claims measure the invention." In re Lang, 644 F.2d 856, 862, 209 USPQ 288, 293 (CCPA 1981). Moreover it is incumbent on Examiner to identify wherein each and every facet of the claimed invention is disclosed in the reference. Lindemann

Maschinen-fabrik Gmbh v. American Hoist and Derrick Co., 730 F.2d 1452, 221 USPQ 481 (Fed. Cir. 1984). Further, the reference must describe the invention as claimed sufficiently to have placed a person of ordinary skill in the art in possession of the invention. An inherent property has to flow naturally from what is taught in a reference In re Oelrich, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981).

"Rejections under 35 U.S.C. §102 are proper only when the claimed subject matter *is* identically disclosed or described in the "'prior art'" . . .the [r]eference must clearly and unequivocally disclose the claimed compound or direct those skilled in the art to the compound without *any* need for picking, choosing, and combining various disclosures not directly related to each other by the teachings in the cited references. Such picking and choosing may be entirely proper when making a rejection of a 103, obviousness rejection, where the applicant must be afforded an opportunity to rebut with objective evidence any inference of obviousness which may arise from the *similarity* of the subject matter which he claims to the prior art, but it has no place in the making of a 102, anticipation rejection." (Emphasis in original). *In re Arkey, Eardly, and Long*, 455 F.2d 586, 172 USPQ 524 (CCPA, 1972).

THE CLAIMS

Claim 8 is directed to a method for assigning function to the product of a sample nucleotide sequence. The steps of the method include:

> a) without any intervening bacterial cloning steps, obtaining and expressing one or more members of an oligonucleotide family as individual transcription products in a plurality of recombinant non-bacterial host cells, wherein:
>
> the coding sequences for each individual transcription product encodes an antisense nucleic acid that, when expressed as RNA, binds to mRNA transcribed from a target nucleic acid molecule that comprises the nucleotide sequence of the sample nucleic acid;

the function of the nucleotide sequence or encoded product is unknown; and

expression of one or more of the individual transcription products inhibits production of a product of the mRNA; and

b) analyzing phenotypic changes in the resulting host cells to thereby identify a corresponding change in function, whereby, based upon the corresponding change in function, a function is assigned to the nucleotide sequence of the sample nucleic acid.

Dependent claims 9-14 specify particulars, such as the nature of the function (*e.g.*, a physiological function, an enzymatic function, protein synthesis, expression of a biological factor or a regulatory effector function) and whether the function is changed directly. Retained claims 58-69 specify particulars, such as the introduction of members of the oligonucleotide family into an expression vector (*e.g.*, a plasmid or a virus), the type of sample nucleic acid (*e.g.*, genomic DNA, cDNA, an EST or RNA) or that the methods are performed in high-throughput format. Thus, all of the instantly claimed methods are directed to assigning a function to a nucleotide sequence of a sample nucleic acid. The claimed methods assign a previously unknown function to a sample nucleic acid of known sequence based on detection and analysis of a cellular phenotypic change.

ANALYSIS

Differences between the claims and the disclosure of Beach *et al.* (US 6,255,071)

Beach *et al.*

Beach *et al.* discloses methods for identifying nucleic acid molecules that inhibit or influence a mammalian cellular function of interest. One method disclosed by Beach *et al.* involves the identification of nucleic acid molecules that modulate a known function of a known target mammalian gene. In this method, libraries of nucleic acid molecules derived from the target gene sequence are

screened for those nucleic acid molecules that alter the known function of the target gene (*e.g.*, inhibit gene expression). The nucleic acid molecules screened for in this manner represent newly identified sequences that can be used as functional knockouts of the gene of interest (column 22, lines 49-51).

For example, in Example 15 (beginning at column 48, line 5), Beach *et al.* describes the preparation of a single gene antisense library of nucleic acid molecules that are derived from a transcript encoding the target gene. This library is screened for nucleic acid molecules that inhibit the expression of the target gene by monitoring the level of fluorescence of a reporter gene that has been fused to the target gene. Thus, the library is screened to identify new nucleic acid sequences that can be used to inhibit the function of the target gene by blocking its expression.

An alternative method disclosed by Beach *et al.* describes the identification of nucleic acid molecules that modulate a known cellular phenotype (column 24, lines 2-37). Here, the modulation of the known cellular phenotype is indicative of an alteration in the expression of an unknown gene. This method requires screening of a random test nucleic acid or a library of random test nucleic acids, such as a cDNA library. Nucleic acid molecules that modulate a particular phenotype as determined by this screen represent newly identified sequences that effect a particular change in expression of an unknown gene corresponding to the phenotype.

For example, in Example 16 (beginning at column 48, line 53), Beach *et al.* discloses methods for the *in vitro* screening of a cDNA library for nucleic acid molecules that induce a known phenotype, telomerase activity, in human mammary epithelial cells (HMECs). Here, pools of cDNAs (in the sense or antisense orientation) are introduced into HMEC cells and an individual clone that demonstrates an induction of telomerase activity is isolated (column 48, line 53,

through column 49, line 20). The sequence of the isolated nucleic acid molecule represents a newly identified sequence from the cDNA library that induces a particular phenotype, namely, telomerase activity.

Both methods described by Beach *et al.* involve the identification of new nucleic acid sequences that effect a change in phenotype by interacting with either a known or unknown gene. Beach *et al.* provides a method for understanding of cellular function by identifying either: (1) for known genes of known function, nucleic acid sequences derived from the known gene that modulate the known function; or (2) for unknown genes, nucleic acid sequences from a random "test" pool that modulate a known phenotype associated with the unknown gene. Both methods involve identifying nucleic acid sequences that modulate a target cellular effect of a known or unknown gene.

Neither method assigns a function to a known sample nucleic acid sequence whose function is previously unknown.

Beach *et al.* does not disclose methods for **assigning function** to a product encoded by a sample nucleic acid of known sequence where the expression of the sample nucleic acid is inhibited by a member of an oligonucleotide family as described in the instant application. Rather, Beach *et al.* discloses methods for the identification of heretofore unknown nucleic acid sequences that either: (1) inhibit the expression of a known gene; or (2) induce a particular phenotype by inhibiting expression of an unknown gene.

Beach *et al.* also does not disclose the subject matter described in dependent claims 9-14 and retained claims 58-69, such as various types of functions (*e.g.*, a physiological function, an enzymatic function, protein synthesis, expression of a biological factor or a regulatory effector function), various types of known sample nucleic acids (*e.g.*, genomic DNA, cDNA, an EST or RNA) or that the methods can be performed in high-throughput format. Thus,

Beach *et al.* does not disclose every element of the claimed subject matter because Beach *et al.* does not provide a method that assign a previously unknown function to a nucleic sequence present in a sample.

Further, Beach *et al.* does not: (1) design and prepare an oligonucleotide family containing related members of a known sequence with unknown function as described in the instant application; (2) express the members of the aforementioned oligonucleotide family in a host cell; (3) detect and analyze phenotypic changes within the host cell; and (4) assign a previously unknown function to the sample nucleic acid of known sequence based upon the observed phenotypic change. Therefore, Beach *et al.* does not anticipate any of claims 8-14 or retained claims 58-69 of added claims 70-72, which are directed to the assignment of a previously unknown function to a sample nucleic acid of known sequence.

* * *

In view of the above amendments and remarks, reconsideration and allowance of the application are respectfully requested.

Respectfully submitted,
HELLER EHRMAN WHITE & McAULIFFE LLP

By: _____
Stephane Seidman
Registration No. 33,779

Attorney Docket No. 24743-2307US
Address all correspondence to:
HELLER EHRMAN WHITE & McAULIFFE LLP
4350 La Jolla Village Drive, 6th Floor
San Diego, CA 92122
Telephone: 858 450-8400
Facsimile: 858 587-5360
email:sseidman@HEWM.com

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: KECK *et al.*

Serial No.: 09/601,997
Conf. No.: 5984; Customer No. 24961

Filing Date: December 15, 2000

For: ***NON-BACTERIAL CLONING IN DELIVERY AND EXPRESSION OF NUCLEIC ACIDS***

Art Unit: 1635

Examiner: Epps, Janet L.

CERTIFICATE OF MAILING BY "EXPRESS MAIL"
"Express Mail" Mailing Label Number
EV 338076925 US
Date of Deposit May 7, 2003

I hereby certify that this paper and the attached papers are being deposited with the United States Postal "Express Mail Post Office to Addressee" Service under 37 C.F.R. §1.10 on the date indicated above and addressed to:

Commissioner for Patents
U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

05/07/2003
Date

Michael Lough

MARKED UP CLAIMS (37 C.F.R. § 1.121)

Please amend claims 8, 14, 58, 62 and 64-69 as follows:

8. (Thrice Amended) A method of assigning a function to a product coded for by a [sample] nucleotide sequence of a sample nucleic acid, said method comprising:

a) without any intervening bacterial cloning [steps,,]steps, obtaining and expressing one or more members of an oligonucleotide family as individual transcription products in a plurality of recombinant non-bacterial host cells, wherein:

the coding sequences for each individual transcription product encodes an antisense nucleic acid that, when expressed as [RNA]RNA, binds to mRNA transcribed from a target nucleic acid molecule that comprises [a]the nucleotide sequence of the sample nucleic acid;

the identity of the nucleotide sequence or an encoded product is known, butthe function of the nucleotide sequence or encoded product is unknown; and

expression of one or more of the individual transcription products inhibits production of a product of the mRNA; and

b) analyzing phenotypic changes in the resulting host cells to thereby identify [one or more altered function(s)]a corresponding change in function,[; and

c) obtaining a nucleotide sequence of said target nucleic acid,] whereby, based upon the [altered]corresponding change in function, a function is assigned to [a sample nucleotide sequence]the nucleotide sequence of the sample nucleic acid.

14. (Amended) The method according to Claim 8, wherein said function is [altered]changed directly.

58. (Amended) The method of claim [1]8, wherein the one or more members of the oligonucleotide family are introduced into expression vectors, which are introduced into the host cells, wherein the expression vectors comprise:

double-stranded DNA, comprising:

a sense strand and an antisense strand, wherein the sense strand codes for an antisense strand that, when expressed as RNA binds to an mRNA sequence transcribed from the target nucleic acid sequence so that expression of a product the target nucleic acid is inhibited; and

means for determining directionality of expression, wherein the product is associated with at least one phenotypic property of a host cell containing the mRNA sequence; and wherein the expression vector is for expression in non-bacterial host cells.

62. (Amended) The method of [any one of] claim [1]58, wherein the expression vector is a plasmid or a virus for expression in non-bacterial host cells.

64. (Amended) The method of claim [1]58, wherein the expression vector is transfected directly into mammalian cells.

65. (Amended) The method of claim [1]8, wherein the sample nucleic acid is genomic DNA, cDNA, an expressed sequence tag (EST) or RNA.

66. (Amended) The method of claim [1]8, wherein the family contains between 3 and 20 members.

67. (Amended) The method of claim [1]8, wherein each member of the family is designed to inhibit the production of a product of the target nucleic acid molecule.

68. (Amended) The method of [claims 1]claim 8 that is performed in a high throughput format, whereby all members of a family are assessed in a single experiment.

69. (Amended) The method of claim [1]8 that is performed in a high throughput format, whereby a plurality of different target nucleic acid molecules and/or sample nucleotide sequences are assessed.